

RECENT PROGRESS IN THE SERUM DIAGNOSIS OF SYPHILIS*

HOWARD FOX, M.D.
NEW YORK

In reviewing the literature on the serum diagnosis of syphilis that has appeared since the last meeting of this Association, I have attempted to call attention to the progress that has been made during the year rather than to discuss at length the present status of our knowledge of the subject. The continued interest in the Wassermann reaction, and in various other serodiagnostic tests for syphilis, is shown by the large number of serious researches and clinical reports that have appeared during the past year. Four excellent books on the subject have been published in German, English and French. It was proper that the first of these should have been written by one of the discoverers of the Wassermann reaction, Carl Bruck,¹ whose personal experience with the test has been enormous. He has given a most excellent presentation of the whole subject from both the theoretical and practical standpoints. Noguchi² has also written a book of great value, in which special attention is devoted to his own modification. Interesting booklets have also been published by Gastou and Girauld³ in France, and by Mulzer⁴ in Germany.

VARIOUS SERODIAGNOSTIC TESTS

Before discussing the more important subject of the Wassermann reaction I should like to call attention to

* Read in the Section on Dermatology of the American Medical Association, at the Sixty-first Annual Session, held at St. Louis, June, 1910.

1. Bruck, C.: *Die Serodiagnose der Syphilis*, Julius Springer, Berlin, 1909.

2. Noguchi, H.: *Serum Diagnosis of Syphilis, and the Butyric Acid Test for Syphilis*, J. B. Lippincott, New York, 1909.

3. Gastou, P., and Girauld, A.: *Guide pratique du diagnostic de la syphilis*, J. B. Baillière et Fils, Paris, 1910.

4. Mulzer, P.: *Praktische Anleitung zur Syphilisdiagnose auf biologischem Wege*, Julius Springer, Berlin, 1910.

some of the serodiagnostic tests for syphilis, depending on principles other than those of complement-fixation. I had supposed that the status of the various precipitation tests for syphilis was fairly well settled at the last meeting of this association. In a paper read on that occasion Wieder and L'Engle,⁵ from experiments with sodium taurocholate and glycocholate, lecithin, taurin and water, concluded that the proportion of positive results in non-syphilitics was too high to make the test of value. This seemed to be the prevailing opinion last year and is, I think, at present, in spite of two recent reports on the subject. Rosenfeld and Tannhauser,⁶ in a series of 131 cases, obtained results that compared favorably with those of the Wassermann test. Tanton and Combe,⁷ from an examination of sixteen cases, concluded that the precipitation method was equally specific, in addition to being much simpler than the Wassermann reaction. Sourd and Pagniez,⁸ however, found that the precipitation test gave six positive reactions in non-syphilitic cases, and Paris and Sabaréanu,⁹ from an examination of fifty-three cases, conclude that the test is of no diagnostic value whatever. A similar opinion is expressed by Laub and Novotny¹⁰ in regard to the value of the reaction for pathologic-anatomic diagnosis, their experiments including a simultaneous test of ninety-eight cadaver serums. Unfavorable results are also reported by Minelli and Gavazzeni.¹¹ In all of the above communications the test with glycocholate of soda was the one employed.

Since the publication of Noguchi and Moore¹² last July on the butyric acid test in the metasyphilitic and

5. Wieder, H. S., and L'Engle, E. M.: Some Studies of the Precipitation Test for Syphilis, *THE JOURNAL A. M. A.*, Nov. 6, 1909, p. 1535.

6. Rosenfeld, F., and Tannhauser: Die Serodiagnose der Lues mittels Ausflockung durch glykocholsaures Natrium, *Deutsch. med. Wchnschr.*, 1910, xxxvi, 165.

7. Tanton and Combe, E.: Le séro-diagnostic de la syphilis par la méthode de Porges, *Compt. rend. Soc. de biol.*, 1910, lxxviii, 436.

8. Le Sourd, L., and Pagniez, P.: La réaction précipitante du sérum syphilitique vis-à-vis des solutions de glycocholate de soude, *Compt. rend. Soc. de biol.*, 1909, lxxvii, 84.

9. Paris, A., and Sabaréanu: La séro-précipitation chez les syphilitiques par le glycocholate de soude, *Compt. rend. Soc. de biol.*, 1910, lxxviii, 290.

10. Laub, M., and Novotny, J.: Ueber die Brauchbarkeit der Porges'schen Ausflockungsreaktion für die Diagnose der Lues an Leichen, *Ztsch. f. Immunitätsforsch.*, 1909, iii, 394.

11. Minelli, S., and Gavazzeni, G. A.: Il metodo di Porges nella sierodiagnosi della sifilide, *Gazz. med. Ital.*, 1909, ix, 191.

12. Noguchi, H., and Moore, J. W.: The Butyric Acid Test for Syphilis in the Diagnosis of Metasyphilitic and Other Nervous Diseases, *Jour. Exper. Med.*, 1909, xi, 605.

nervous diseases, nothing further has been written on this method. In their experiments the writers found that the test was not absolutely specific, positive reactions having been obtained in two out of thirty-seven psychoses not in any way related to syphilis. In his book on serum diagnosis Noguchi states that the butyric acid test while not entirely specific, is at times more valuable than the Wassermann reaction in excluding syphilis, for instance, when the reaction is negative.

Assuming that the *modus operandi* of the Wassermann reaction depends on a precipitation, Jacobsthal¹³ suggests a method which he terms the "optic serodiagnosis of syphilis." The patient's serum is mixed with alcoholic extract of syphilitic liver in the proportion of 1 to 10 and the resulting precipitate is examined with the dark-field illuminator. A strong positive reaction appears as a clumpy preeipitate, a weak positive reaction as a small conglomeration of little fat particles, while a negative is shown as a thick emulsion of very fine dancing fat particles. In comparing his method with the Wassermann reaction Jacobsthal claims that, after having acquired the necessary experience, his results with the two tests were identical.

It can hardly be of more than historical interest to discuss the color reaction suggested by Schürmann,¹⁴ that has been so thoroughly discredited by subsequent experimentation. Indeed, it seems strange that so much has been written on the subject when it seemed almost from the start that the method was valueless. A few words about this proposed method may aid in preventing others from further experimentation. Schürmann thought that there might possibly be some substance in the blood of syphilitics whose presence could be recognized by a color reaction. It occurred to him that lactic acid might play a part in the reaction, as this substance had been present in one of his most reliable extracts. His first experience with Uffelmann's reagent being unsuccessful, he was led to use perhydrol in combination with phenol and chlorid of iron. According to Schürmann, when the reagents were mixed with normal serum a light green color appeared at the upper portion of the mixture. This either disappeared or changed to a light

13. Jacobsthal, E.: Die optische Serodiagnose der Syphilis, München, med. Wchnschr., 1909, lvi, 2607.

14. Schürmann, W.: Luesnachweis durch Farbenreaktion, Deutsch. med. Wchnschr., 1909, xxxv, 616.

green tint on shaking, the solution remaining clear. When syphilitic serum was used a blackish-brown dull tint appeared almost immediately, the solution giving the impression of a thick mixture.

Employing his method in eighty-four cases simultaneously with the Wassermann test, Schürmann claimed to have obtained identical results. In a comparison of the Schürmann with the Wassermann test in 154 cases of undoubted syphilis Meirowsky¹⁵ obtained 62.3 per cent. of positive reactions for the Wassermann test as opposed to 11.9 per cent. for the Schürmann method. The list of investigators whose results have been unfavorable, and who conclude that the test is of no clinical value, includes Biach,¹⁶ Bonola,¹⁷ Braunstein,¹⁸ Bruck,¹ Galambos,¹⁹ Roth and Goldner,²⁰ Schminke and Stoerber,²¹ C. Stern,²² Stühmer,²³ Symanski, Hirschbruch and Gardiewski.²⁴ According to the chemical examination of Braunstein,¹⁸ the reaction is a process of oxidation, the perhydrol oxidizing the phenol by means of the iron chlorid.

Interesting results have been obtained by Nicolas, Favre and Gautier²⁵ with dermic and intradermic reactions in syphilis, analogous to the reaction caused by tuberculin for the diagnosis of tuberculosis. For this purpose the experimenters used a concentrated glycerinated extract of liver of syphilitic fetus which they termed "syphiline." When this extract was used by the dermic method (as in the von Pirquet test), no change

15. Meirowsky, E.: Die Schürmannsche Methode des Luesnachweises mittels Farbenreaktion, Deutsch. med. Wchnschr., 1909, xxxv, 937.

16. Biach, M.: Ueber Luesnachweis durch Farbenreaktion, Wien. klin. Wchnschr., 1909, xxi, 606.

17. Bonola, F.: Sulla reazione cromatica di Schürmann per la sierodiagnosi della sifilide, Riforma med., 1909, xxv, 682.

18. Braunstein, A.: Ueber die Schürmannsche Farbenreaktion bei Lues, Ztschr. f. klin. med., 1909, lxxviii, 345.

19. Galambos, A.: Ueber den Wert der Farbenreaktion bei Lues, Deutsch. med. Wchnschr., 1909, xxxv, 976.

20. Roth, A., and Goldner, V.: Ueber die Farbenreaktion bei Lues, Orvosi hetil., 1909, No. 19. (Review in Monatsh. f. prakt. Dermat., 1909, l, 129.)

21. Schminke and Stoerber: Zur Kritik der Schürmannschen Farbenreaktion bei Lues, Deutsch. med. Wchnschr., 1909, xxxv, 937.

22. Stern, C.: Ueber die Bewertung einer Serum-Farbenreaktion zum Luesnachweis, Berl. klin. Wchnschr., 1909, xli, 1068.

23. Stühmer, A.: Luesnachweis durch Farbenreaktion, Fortsch. d. Med., 1909, xxvii, 714.

24. Symanski, Hirschbruch and Gardiewski: Luesnachweis durch Farbenreaktion, Berl. klin. Wchnschr., 1909, xli, 874.

25. Nicolas, J., Favre, M., and Gautier, C.: Intradermoréaction et cutréaction avec la syphiline chez les syphilitiques, Compt. rend. Soc. de biol., 1910, lxxviii, 257.

was noted. When, however, the extract was injected intradermically a reaction consisting of redness and nodular infiltration was obtained in a large proportion of the twelve cases examined. In a second contribution the same authors²⁶ give the results in fifty cases, of a comparison of their test with the Wassermann reaction. The results were in agreement in forty-two cases. Of the remaining eight cases five seemed to favor the correctness of the diagnosis by the intradermic test, while one favored the Wassermann method.

The relation of the Wassermann test to the antitryptic power of the blood in syphilis was studied by Fuerstenberg and Trebing.²⁷ The determination of the antitryptic index (using a modified method of Müller and Jochman) was made simultaneously with the Wassermann method in sixty-one cases of syphilis and other diseases. It was found that in cases of undoubted syphilis giving a positive reaction the antitryptic titer or index was never increased. In the majority of cases it was diminished. Whether this test will prove of value, from the fact that an increased antitryptic titer would seem to exclude syphilis, can be judged only after further investigation with this method.

According to Achard, Benard and Gagneux,²⁸ the so-called leukodiagnosis, which is based on specific sensitiveness of leukocytes *in vitro* to certain normal or pathologic products, may also be applied to syphilis. The specific principle used by these writers was a glycerinated extract of spleen of a congenitally syphilitic infant containing *Spirochata pallida*. The strongest influence on the leukocytes was obtained with a 5 per cent. dilution of the extract. In this strength the leukocytic activity was found to be more or less increased in syphilis, while it was not at all influenced in healthy subjects. It was found in their investigations that the strongest reactions correspond to the period of early secondary syphilis, while the reactions were weaker in hereditary manifestations of the disease and in tabes and paresis.

26. Nicolas, J., Favre, M., and Charlet, L.: Comparaison des résultats fournis par l'intradermo-réaction à la syphiline et par la séro-réaction de Wassermann, Bull. et mém. Soc. méd. d. hôp. de Paris, 1910, xxvii, 440.

27. Fuerstenberg, A., and Trebing, J.: Die Luesreaktion in ihren Beziehungen zur antitryptischen Kraft des menschlichen Blutes, Berl. klin. Wchnschr., 1909, xli, 1357.

28. Achard, C., Benard, H., and Gagneux, C.: Leueo-Diagnostie de la Syphilis, Compt. rend. Soc. de biol., 1910, lxxviii, 323.

The reaction first described by Much and Holzmann was tried by Hamburger²⁹ in twenty-two cases of syphilis simultaneously with the Wassermann test. The results obtained were entirely contradictory, the writer concluding that the test has no value in syphilis. The reaction which has previously been seen only in certain insane persons, especially dementia præcox, consists in an inhibitory action to the hemolysing power of cobra venom.

In experimenting with various hemolysing agents in different diseases it was found by Richard Weil³⁰ that the erythrocytes of syphilitics were especially resistant to the hemolysing power of cobra venom. This fact has been utilized as the basis of a diagnostic test for syphilis that promises to be of considerable value. The technic of the procedure is as follows: Blood is drawn into a 2 per cent. solution of sodium citrate, washed and made into a 4 per cent. suspension in normal salt solution. It is then tested on the following day. Equal amounts of venom at 1 to 800 and 1 to 1,500 are added and after one hour of incubation the results are read. It has been found that syphilitic cells resist a solution of 1 to 1,800; that is, twice as strong as that which destroys the control. The reaction was found to be marked in 90 per cent. of the cases of syphilis, the percentage of positive reactions being smaller in tabes than in paresis. In several non-syphilitic affections in which the Wassermann test was positive (three cases of scarlatina, two cases of polycythemia and one case of scleroderma) the Weil test showed a negative reaction. Some advantages which Weil claims for his test are that it can be used in cases of jaundice. It is positive for some time after mercurial treatment has abolished the Wassermann reaction. It is finally positive in a very large percentage of old quiescent cases in which the Wassermann test is negative. Dr. Weil informs me in a personal communication that he considers his test too delicate for general use, as a very considerable amount of practice is required in order to interpret the results obtained.

29. Hamburger, J.: Ueber die Beeinflussung der Kobra-Gift-Hämolyse durch Seren von Haut- und Geschlechtskrankheiten, *Dermat. Ztschr.*, 1909, xvi, 785.

30. Weil, R.: The Resistance of Human Erythrocytes to Cobra Venom., *Jour. Infect. Dis.*, 1909, vi, 688; The Variation in the Resistance of Human Erythrocytes to Disease to Hemolysins, with Especial Reference to Syphilis, *Proc. Soc. Exper. Biol. and Med.* 1910, vii, 2.

The meiostagmin reaction suggested by Ascoli and used by him as a diagnostic procedure in typhoid fever has been applied by Izar³¹ to syphilis. The test is a physico-chemical reaction of immunity depending on a change in surface tension of the fluids employed. When the serum of a syphilitic is mixed with its corresponding antigen and placed in the thermostat for two hours there is a diminution in surface tension as shown by an increase in the number of drops of a measured amount of the fluids. According to Izar the test was found to be entirely specific. A positive reaction was obtained in twelve cases of syphilis, while all of the non-syphilitic cases gave negative results, including two cases of leprosy in which the Wassermann reaction had been positive.

WASSERMANN TEST AND ITS MODIFICATIONS

In reviewing the recent progress of the Wassermann reaction I should first like to discuss some of the more important and practical contributions that relate to the technic of the method. A simple means of obtaining the patient's blood for examination has been suggested by Muck.³² The superficial veins of the neck are compressed by Bier's method and the mucous membrane of the anterior portion of the septum is scratched with a small needle or knife. In about three minutes as much as 20 c.c. of blood can be readily secured. The bleeding stops on removal of the compression, or on introduction of a pledget of cotton into the nose. Another method of obtaining blood where a venepuncture is difficult or not desirable, as in infants, is suggested by Somani.³³ After scarifying the skin he applies a cupping apparatus with an outlet below attached to a test-tube to receive the blood, and a suction-pump attached in the center. To this and other cupping methods Mulzer makes the objection that the apparatus is difficult to sterilize and that unsightly scars are left which if the method were widely adopted and known to the laity might at times prove compromising.

31. Izar, G.: Ueber eine spezifische Eigenschaft luettischer Blutsera, München. med. Wehnsehr., 1910, lvii, 182.

32. Muck, O.: Die Schleimhaut der Nasenseidewand eine besonders geeignete Stelle für die Blutentnahme zu der Wassermannschen Reaktion und zu anderen serologischen Untersuchungszwecken, München. med. Wehnsehr., 1909, lvi, 2321.

33. Somani, B. P.: Quantitative Bestimmung der luettischen Serumveränderung mittels der Reaktion von Wassermanu, Neisser und Bruck, Arch. f. Dermat. u. Syph., 1909, xeviii, 73.

Finkelstein³⁴ has devised an apparatus for determining quantitatively the strength of a positive reaction. He uses a glass funnel (of a shape to fit a centrifuge), at the bottom of which a graduated tube is fused. The undissolved corpuscles of the case to be examined and of the known positive cases are poured into two separate funnels, which are then centrifugalized and the result mathematically read. A somewhat similar apparatus has been recently suggested by Heimann.³⁵

As yet no one has produced the much-desired artificial antigen which shall prove as reliable and specific as the various organ extracts now in use. The artificial antigen of Sachs and Rondoni has, however, been found in the hands of Eisenberg and Nitsch³⁶ to be the equal of organ extracts, while unfavorable results in its use were obtained by Isabolinsky.³⁷ An artificial antigen has been suggested by Schürmann³⁸ which, in addition to lecithin, contains glycerophosphate of sodium and ammonium vanadate. This has been tested by Rajchman and Zygmunt³⁹ with disappointing results. They conclude that artificially prepared antigens are not reliable substitutes for alcoholic organ extracts, as in weak doses they often fail to give positive reactions with syphilitic serums and in stronger doses give a positive reaction with normal serums.

It was recently pointed out by Wechselmann⁴⁰ that the failure to obtain higher percentages by positive reactions in cases of undoubted syphilis might be due to interference from the presence of complementoids. By removing these disturbing bodies, by shaking the serum with barium sulphate, better results were obtained than with the regular Wassermann method. This procedure

34. Finkelstein, J. A.: Zur Technik der Wassermannschen Reaktion, Berl. klin. Wchnschr., 1909, xlv, 1611.

35. Heimann, W. J.: A Method for the Mathematical Reading of the Original Wassermann Reaction, THE JOURNAL A. M. A., May 21, 1910, p. 1684.

36. Eisenberg, R., and Nitsch, R.: Ueber Wassermannsche Reaktion mit künstlicher Antigen, Przegląd Lekarski, 1909, No. 32. (Reviewed in Monatsh. f. prakt. Dermat., 1909, I, 131.)

37. Isabolinsky, M.: Weitere Untersuchungen zur Theorie und Praxis der Serodiagnostik bei Syphilis, Ztschr. f. Immunitätsforsch., 1909, III, 143.

38. Schürmann, W.: Ein künstlicher Extrakt zur Anstellung der Luesreaktion, Med. Klin., 1909, v, 627.

39. Rajchman, L., and Zygmunt, S.: Praktische Bemerkungen zu der Frage der Wassermannschen Reaktion, Przegląd Lekarski, 1909, No. 25. (Reviewed in Monatsh. f. prakt. Dermat., 1909, I, 138.)

40. Wechselmann: Ueber Verschleierung der Wassermannschen Reaktion durch Komplementoidverstopfung, Ztschr. f. Immunitätsforsch., 1909, III, 525.

has been tried by Lange⁴¹ with strikingly good results in a series of 800 cases, in which both methods were simultaneously performed. In 551 syphilitic serums the Wechsellmann test yielded 85 per cent. of positive reactions, as against 77 per cent. for the Wassermann method. In non-syphilitic control cases the Wechsellmann test gave only negative reactions. Shaking the serum with barium sulphate not only adds to the delicacy of the test, but also destroys the complement, making it unnecessary to inactivate the patient's serum by heating to 56 C. for a half hour. Lange, therefore, at the present time uses the barium sulphate treatment of the serum as a substitute for inactivation by heat.

In order that positive and negative control serums may always be at hand Hecht⁴² recommended that they be preserved by means of drying. Small amounts, such as 0.5 c.c., are dried in watch crystals. When the serum is needed it is dissolved in an equal amount of salt solution, after which equal amounts of distilled water are added. The combination of salt solution and water is advised, as when distilled water is added to the dried serum certain substances (possibly globulins) remain undissolved and float about in the mixture as cloudy masses.

According to Blanck and Friedmann⁴³ alcoholic extracts of syphilitic liver at times lose their usefulness for the Wassermann reaction by being kept in the ice-chest or in a cold solution. They found that in some cases this could be remedied by allowing the extract to remain in a thermostat for several days. To preserve their efficiency best it is advised to keep extracts in a warm room.

Further researches on the feasibility of using urine in place of serum for the Wassermann reaction have been made by Pollio.⁴⁴ His conclusions are similar to those of Höhne, that the use of the urine has no practical value, as too large a percentage of positive reactions are given in non-syphilitic cases. Even Blumenthal and Wile, who first experimented with urine, admitted that

41. Lange, C.: Ergebnisse der Wassermannschen Reaktion bei Vorbehandlung der Sera mit Baryumsulfat nach Wechsellmann, Deutsch. med. Wchnschr., 1910, xxxv, 217.

42. Hecht, H.: Zur Technik der Seroreaktion bei Syphilis, Ztschr. f. Immunitätsforsch., 1910, v, 572.

43. Blauek and Friedmann: Ueber thermoreversible Zustandsänderungen der bei der Wassermannschen Reaktion verwendete alkoholischen Leberextrakte, Ztschr. f. Immunitätsforsch., 1909, iii, 108.

44. Pollio, G.: La reazione di Wassermann eseguita colle urine ha valore pratico, Riforma med., xxv, 231.

it was not quite as reliable as blood-serum for the Wassermann test. Bauer and Hirsch⁴⁵ conclude that in positive reactions obtained by using urine the inhibition of hemolysis is due to the globulin fraction of the urine. They obtained negative results in non-syphilitic urine containing albumin and in syphilitic urine containing no albumin, or albumin in small amounts.

In a discussion by Stern⁴⁶ of uncertain and paradoxical reactions that are so often obtained by every serologist, some of the rules are given that are at present followed in the laboratory of the Neisser clinic at Breslau. Every serum is tested both by the original Wassermann and by the Stern method; that is, in both active and inactive condition. When the results are not in accord the serums of the cases that are clinically doubtful are tested once or more times, using various extracts known to be reliable. The same procedure is followed in serums giving a partial inhibition of hemolysis and in serums of apparently healthy persons giving a positive reaction.

That the Wassermann reaction as originally performed is not absolutely satisfactory from either the theoretical or practical standpoint is apparent from the many attempts that have been made to improve and simplify the test. Of the different methods depending on the principle of complement-fixation there are eight which might be termed systems, which were published before June, 1909. The principles on which these different systems are constructed are very plainly shown in a comparative table by Noguchi in his book on serum diagnosis.

Since last June another "system" has been added to the list by Foix,⁴⁷ who suggests the use of rabbit's blood for the indicator in place of sheep's blood. During the past year the modifications⁴⁸ of Bauer, Tschernogub-

45. Bauer, R., and Hirsch, A.: *Beitrag zum Wesen der Wassermannschen Reaktion*. *Wien klin. Wchnschr.*, 1910, xxiii, 6.

46. Stern, M.: *Ueber die Bewertung der unsicheren und "paradoxen" Reaktion bei der serodiagnostischen Untersuchung der Syphilis*, *Ztschr. f. Immunitätsforsch.*, 1910, v, 201.

47. Foix, C. H.: *Sur une technique simplifiée de réaction de fixation*, *Compt. rend. Soc. de biol.*, 1909, lxxvii, 171.

48. The modification of Bauer dispenses with immune (artificial) amboceptor and depends on the natural antishoop amboceptor present in the patient's serum. The Hecht method dispenses not only with the immune amboceptor but also with the guinea-pig complement, utilizing the complement normally present in the patient's serum. Stern in her modification also relies on human complement, but unlike Hecht uses the immune amboceptor. Tschernogubow in his second method employs the red corpuscles of the guinea-pig instead of the sheep as his indicator. He also makes use of human complement. Noguchi employs human corpuscles as the indicator, guinea-pig serum for complement, and antihuman amboceptor.

bow (second method), and more especially those of Hecht and Stern, have been the subject of a good deal of investigation in Europe, while the method of Noguchi has received especial attention in America. The final word is yet to be pronounced on these various modifications, as there is not yet an absolute opinion as to their value.

Very favorable results with the Hecht test are reported by König,⁴⁹ who finds it superior to both the original method and that of Margarete Stern. In a more recent communication on the method of Hecht, the same writer⁵⁰ concludes that it fulfils all the requirements of any modification, which are that: 1. It must have a scientific basis. 2. It must be simpler and more delicate than the original method. 3. It should never give erroneous results. Demanche and Ménard⁵¹ conclude that the results of the Hecht test are practically as reliable as those of the original method. Scholtz⁵² speaks of the test as simple and reliable. From his experience with 500 cases performed simultaneously with the Wassermann test, Werther⁵³ considers the Hecht method preferable, as it gives less often an incomplete inhibition; e. g., doubtful results. Favorable expressions of opinion on this method are also given by Stanculéanu and Liebreich⁵⁴ and by Sabrazes and Eckenstein.⁵⁵ Unsatisfactory results with the Hecht and with the Bauer test are reported by Hügel and Reute,⁵⁶ while both of these methods, as well as those of Stern and Tschernogubow, are condemned by Isabolinsky as giving less certain results than the Wassermann test.

49. König: Warum ist die Hechtsche Modifikation der Wassermannschen Luesreaktion besser und der Sternschen Modifikation vorzuziehen? Wien. klin. Wchnschr., 1909, xxii, 1127.

50. König: Ueber die Hechtsche Modifikation der Wassermannschen Seroreaktion, Deutsch. med. Wchnschr., 1910, xxxvi, 506.

51. Demanche, R., and Ménard, P. J.: Valeur de la méthode de Hecht pour le séro-diagnostic de la syphilis; comparaison avec la réaction de Wassermann, Compt. rend. Soc. de biol., 1910, lxxviii, 714.

52. Scholtz, W.: Ueber die jetzige Bedeutung der Wassermann Neisserschen Reaktion für die Diagnose und Therapie der Syphilis, Klin.-therap. Wchnschr., 1909, xvi, 1190.

53. Werther: Ueber das Wesen und den Wert der Wassermannschen Reaktion und 500 eigene Untersuchungen mit der Hechtschen Modifikation, Monatsh. f. prakt. Dermat., 1910, I, 147.

54. Stanculéanu, G., and Liebreich, N. E.: Die Anwendung der Methode von Bauer-Hecht für die Serumdiagnose bei Augenerkrankungen, Revista stîintelor Med., 1909.

55. Sabrazès, J., and Eckenstein, K.: Note on a Simple Method of Fixation of the Complement in Syphilis, Lancet, London, 1910, cxxxviii, 233.

56. Hügel and Reute: Bisherige Erfahrungen über die Serodiagnostik der Syphilis an der dermatologischen Universitätsklinik zu Strassburg, München. med. Wchnschr., 1910, lvi, 79.

The modification of the Hecht test, still further simplified by Fleming by the use of very small amounts of the ingredients, is condemned on the one hand by Bassett-Smith⁵⁷ and recommended on the other hand by Clemenger.⁵⁸ The former found that hemolysis failed to occur in 30 per cent. of his cases, whereas the latter found only 5 per cent. of failures.

Opinion on the second method proposed by Tschernogubow (the first method having been abandoned) do not seem to entirely agree. Stühmer,⁵⁹ from a comparative examination with the Wassermann test in over 300 cases, concludes that the procedure of Tschernogubow represents a great simplification and that its results are at least as reliable as those given by the original method. On the other hand, Guth⁶⁰ considers the test unsuited for a large laboratory, as the serum must be used immediately after being obtained, while for practicing physicians its performance is difficult.

In reviewing the results obtained with the Stern modification we again find conflicting reports. An unfavorable opinion is given by Kleinschmidt,⁶¹ who thinks that the use of this procedure may lead to errors in diagnosis. In a comparative examination of 200 cases discrepancies were found to the advantage of the Wassermann method in twenty-five cases. In 5 per cent. of the cases there was not sufficient complement to complete the hemolysis. Jacobs and Bachmann⁶² consider the modification of Bauer and Stern unreliable, as they give too many positive reactions in non-syphilitic cases. As treated cases of syphilis generally show an increased amount of amboceptor and complement, they suggest that a positive Bauer reaction (depending on natural amboceptor) or a positive Stern (depending on natural complement) might be considered as giving an unfavorable prognosis

57. Bassett-Smith, P. W.: The Diagnosis of Syphilis by Some Laboratory Methods, Brit. Med. Jour., 1909, II, 377.

58. Clemenger, F. J.: The Diagnosis of Syphilis by Some Laboratory Methods, Brit. Med. Jour., 1909, II, 575.

59. Stühmer, A.: Ueber die von Tschernogubow angegebene Modifikation der Wassermannschen Reaktion, Deutsch. med. Wchnschr., 1909, xxxv, 1517.

60. Guth, H.: Ueber eine (II) von Tschernogubow angegebene Modifikation der Wassermannschen Reaktion, Deutsch. med. Wchnschr., 1909, xxxv, 2319.

61. Kleinschmidt, H.: Ueber die Sternsche Modifikation der Wassermannschen Reaktion, Ztschr. f. Immunitätsforsch., 1909, III, 512.

62. Jacobs, H. C., and Bachmann, E. L.: Sur les différentes modifications de la réaction de Wassermann, Compt. rend. Soc. de biol., 1909, lxxvii, 449.

and indicating prolonged treatment. Schlimpert⁶³ and Meirowsky⁶⁴ warmly recommend the Stern modification, though both of these writers urge that it be performed simultaneously with the original Wassermann method.

NOGUCHI TEST

From this cursory review of the modifications that have been tested with considerable thoroughness abroad it is easy to see that no one method has succeeded in replacing the original procedure of Wassermann. It is unfortunate that the system of Noguchi has not as yet been more seriously considered by our foreign colleagues. In the recent book on serum diagnosis by Gastou and Girauld³ the method is described at some length, although it has been practically performed only in a few cases. Among those of us in America who have had experience with the Noguchi method there is little doubt as to its very great value. The principles of the test, as well as minute instructions for preparing the reagents, are so plainly described in Noguchi's book that it seems strange that the method has not at least been given a trial in some of the foreign laboratories. In a recent contribution Noguchi⁶⁵ has tabulated the work of different American investigators who have experimented with his method, and it may be said that the results speak for themselves. The test has now been tried in over 8,500 cases, many of these in comparison with the regular Wassermann test. Kaplan, who formerly reported 8 per cent. positive reactions in non-syphilitic cases, states that during the past five months no such non-specific reactions have occurred. To meet the objections of Swift, who found thirty-five positive reactions in 201 non-syphilitic cases, Noguchi recently gave a public demonstration of his test at the clinic of the Pennsylvania Hospital. The serums of fifty-nine patients were simultaneously examined by Dr. Noguchi with his method, and by Dr. Swift, using the original technic of Wassermann. The results were absolutely identical.

63. Schlimpert, H.: Beobachtungen bei der Wassermannschen Reaktion, *Deutsch. med. Wchnschr.*, 1909, xxxv, 1368.

64. Meirowsky, E.: Ueber die von M. Stern vorgeschlagene Modifikation der Wassermann-Neisser-Bruckschen Methode, *Berl. klin. Wchnschr.*, 1909, xlv, 1310.

65. Noguchi, H.: Further Studies on the Serum Diagnosis of Syphilis with Especial Reference to the Antihuman Hemolytic System, *Internat. Clin.*, 1910, Series 20, 1, 22.

SPECIFICITY OF WASSERMANN REACTION

The question of the specificity of the Wassermann reaction finally appears to be nearing a solution. The list of non-syphilitic diseases in which a positive reaction can be obtained more or less often is becoming more definitely settled. To this list, which includes leprosy, frambesia, sleeping-sickness, scarlatina, and malaria, must now be added, apparently, lupus erythematosus acutus. Fortunately these conditions do not often present any difficulty in being clinically differentiated from syphilis.

Several communications on the Wassermann reaction in leprosy have recently appeared in which the number of patients examined was fairly large. While agreeing that leprosy in general often gives a positive reaction, they do not agree as to the type of the disease in which the reaction is found. Thus Ehlers and Bourret,⁶⁶ in forty-seven cases of nodular and anesthetic types, found positive reactions in all except two cases. On the other hand, Eliasberg,⁶⁷ in fifty cases, found a much higher proportion of positive reactions in the nodular than in the anesthetic type. My own results⁶⁸ in an examination of sixty patients agree closely with those of Eliasberg, the latter obtaining only three reactions in nineteen anesthetic cases, while I found three reactions in twenty-two cases of this type.

Teissier and Bénard⁶⁹ in 100 cases of scarlatina found the reaction partially or completely positive in 81 per cent. of the cases. The reaction appeared at times as early as the third day and invariably disappeared at the end of convalescence. Using extract of human heart as antigen, Nann-Muscel and Titu⁷⁰ obtained only negative reactions in 12 cases of malaria. In 8 cases the examination was made at the height of the paroxysm when the blood showed the presence of the plasmodium. According to Boehm⁷¹ a positive reaction can be obtained

66. Ehlers and Bourret: Wassermann-Reaktion ved Spedalsked. Ugesk. f. Læger., 1909, No. 49. (Reviewed in Ztschr. f. Immunitätsforsch., 1909, Ref. II, 1007.)

67. Eliasberg, J.: Komplementablenkung bei Lepra mit syphilitischem Antigen, Deutsch. med. Wchnschr., 1909, xxxv, 1922.

68. Fox, H.: The Wassermann and Noguchi Complement-Fixation Test in Leprosy, Am. Jour. Med. Sc., 1910, cxxxix, 725.

69. Teissier, P., and Bénard, R.: Recherches sur la réaction de Wassermann dans la scarlatine, Compt. rend. Soc. de biol., 1910, lxxviii, 272.

70. Nann-Muscel, J., and Titu, V.: La réaction de Wassermann dans la malaria, Compt. rend. Soc. de biol., 1910, lxxviii, 188.

71. Boehm, W.: Malaria und Wassermannsche Reaktion, Malaria, 1909, 1, 191.

in malaria only when the parasites are present in the blood.

In a case of that very rare condition, lupus erythematosus acutus, Reinhart⁷² obtained a positive Wassermann reaction on two different occasions. After the patient's death a positive reaction was obtained from the blood. The autopsy showed no evidence whatever of syphilis. A second case of this disease is reported by Hauck,⁷³ in which on two occasions a positive reaction was found. In this case the patient survived and failed to show the reaction after the acute symptoms had subsided.

Interesting results are recorded by Wolfsohn⁷⁴ from an examination of 50 patients shortly after ether narcosis. A more or less strong positive reaction was found in 13 cases. Two of these patients were syphilitics, in whom the positive reaction persisted, while in the other cases the reaction disappeared in a few days. Wolfsohn concludes that in 22 per cent. of the cases a temporary positive reaction may be present as a result of ether narcosis. He considers his results as a new proof of the biologic non-specificity of the Wassermann test, and of its close relation to lipoid bodies, as the lipoid substances of the brain and cord are the ones that are bound up in the anesthetic and cause narcosis.

The rather surprising statement is made by Gjorgjevic and Savnik⁷⁵ that in examining 24 psoriasis patients giving no history or signs of syphilis, a positive reaction was obtained in 20 cases. As the majority of the reactions were only weakly positive their results will have to be disregarded unless confirmed by other investigators.

Actuated by the report of Bass, who, using lecithin as antigen, found 6 positive reactions in 6 pellagra patients. I examined 30 patients⁷⁶ with this disease with the Noguchi modification. My conclusions were that pellagra

72. Reinhart, A.: Erfahrungen mit der Wassermann-Neisser-Bruckschen Syphilisreaktion, München, med. Wehnschr., lvi, 2092.

73. Hauck: Positiver Ausfall der Wassermann-Neisser-Bruckschen Syphilisreaktion bei Lupus erythematosus acutus, München, med. Wehnschr., 1910, lvii, 17.

74. Wolfsohn, G.: Ueber Wassermannsche Reaktion und Narkose, Deutsch. med. Wehnschr., 1910, xxxvi, 505.

75. Gjorgjevic, G., and Savnik, P.: Ueber die Wassermannsche Reaktion bei Lues und bei Psoriasis vulgaris, Wien. klin. Wehnschr., 1910, xxiii, 626.

76. Fox, H.: The Wassermann Reaction (Noguchi Modification) in Pellagra, New York Jour., 1909, xc, 1206.

does not often give a positive reaction. The few reactions obtained were weak and easily distinguished from those found in cases of syphilis. In a discussion of my paper Dr. Bass stated that in subsequent examinations in which he used organ extracts as antigen his results were similar to mine.

To show finally how small after all is the proportion of positive reactions obtained in non-syphilitic cases, Bruek has collected from the literature 5,028 control cases in which only 59 positive reactions were found. This seems indeed a small number when the possibility of unrecognized latent infection is considered.

The diagnostic value of a positive Wassermann reaction is now almost universally recognized. This is admitted even by Blanck,⁷⁷ one of the severest critics of the test. It may be said in this connection that the most unfavorable criticisms, such as those of Kopp and of Blanck, are usually expressed by men who have had no personal experience in performing the reaction. The question of absorbing interest to the practicing physician as to whether treatment of syphilis can be controlled by means of serum diagnosis, has unfortunately not been settled. It would seem that the problem cannot be solved until we are certain of the significance of a positive reaction. In other words, can it be said that a positive reaction represents the presence somewhere in the body of active syphilitic virus? If this question can be answered affirmatively, it would seem to me that a positive reaction would always indicate antisymphilitic treatment.

In favor of this view Fritz Lesser⁷⁸ has advanced the following arguments: 1. There is a parallelism between the number of positive reactions (49 per cent.) that have been obtained in the later stages of latent syphilis, and the number of cases showing post-mortem evidence of syphilis, in whom during life no manifestations of the disease had been present. 2. There is, further, a parallelism between a positive reaction and clinical manifestations. In many cases the reaction changes from positive to negative with the disappearance of lesions and again becomes positive when relapses occur. 3. Under antisymphilitic treatment the reaction changes from posi-

77. Blanck: Die Bewertung der Wassermannschen Reaktion für die Behandlung der Syphilis, Berl. klin. Wehnschr., 1909, xlv1, 1652.

78. Lesser, F.: Die Behandlung der Syphilis im Lichte der neueren Syphilisforschung, Deutsch. med. Wehnschr., 1910, xxxvi, 116.

tive to negative. In comparing the results of the reaction in cases that had formerly been treated it was found that those that had been thoroughly treated gave a greater number of negative reactions than the ones in whom the treatment had been less thorough.

The significance of a negative reaction from the therapeutic standpoint depends largely on the time that has elapsed since the infection, and since the last injection of mercury. It cannot be judged from the test alone whether we have to deal with latency or with an actual cure of the disease. A negative reaction during the first two or three years seems to be generally considered of small value. If in later years repeated negatives are obtained in a person who shows no clinical manifestations, and who has not recently taken mercury (preferably five months), it would be considered by some that the disease had been cured. It should certainly be looked on as a most favorable result.

FIELD OF APPLICATION OF SERODIAGNOSTIC TEST

The large amount of investigation on the Wassermann reaction during the past year has been productive of some results of very practical value. Much light has been thrown on various questions, such as the problems of syphilitic heredity, prostitution, and the reliability of the test for post-mortem diagnosis. Some valuable contributions relating to the special branches of medicine have also appeared which tend either to prove or to disprove the relationship of certain diseases to syphilis.

Of great importance are the results that have been obtained in diseased conditions of the heart and arteries. Donath⁷⁹ concludes that the syphilitic etiology of aortic insufficiency and aneurism, as well as cases of clinically suspicious mesaortitis, is proven by having obtained a positive Wassermann reaction in 85 per cent. of the cases. Bruckner and Galesco⁸⁰ think that syphilis plays the principal rôle in the etiology of aortic insufficiency, as they found a positive reaction in 17 out of 22 cases. The five patients giving a negative reaction were younger persons, from 14 to 20 years of age, who had suffered from repeated attacks of rheumatism. From an exami-

79. Donath, K.: Ueber die Wassermannsche Reaktion bei Aortenerkrankungen und die Bedeutung der provokatorischen Quecksilberbehandlung für die serologische Diagnose der Lues, Berl. klin. Wchnschr., 1909, xvi, 2015.

80. Bruckner, J., and Galesco: Syphilis et insuffisance aortique, Compt. rend. Soc. de biol., 1910, lxxviii, 74.

nation of twenty-five cases of various lesions of the heart, Oiggaard⁸¹ found positive results in patients suffering from aortic aneurism and uncomplicated aortic insufficiency while negative reactions were obtained in those with lesions of the mitral valve. In 8 out of 9 cases of aortic insufficiency the reaction was also found to be positive by Krefling.⁸²

From a study of 130 cases of disease of the eye in which the Noguchi test was performed, Martin Cohen⁸³ found some interesting results. He considers that "in brain cases with choked discs in which the indications for operations are doubtful and lues is suspected, the presence or absence of the reaction furnishes a valuable confirmatory aid which is speedier or probably more satisfactory than the therapeutic test." He further states that some light may be thrown on the heretofore obscure etiology of retinitis pigmentosa from the large proportion of positive reactions obtained. His conclusion that the Wassermann test is of value in the diagnosis of diseases of the eye is shared by Schumacher⁸⁴ and by Hessberg.⁸⁵

The application of the Wassermann reaction to otologic cases has apparently added to our knowledge of the cause of nerve-deafness. In examining 29 patients with this condition Busch⁸⁶ found 15 strongly positive reactions, or 52 per cent., from which he concludes that syphilis plays a more important rôle in the etiology of nerve-deafness than has previously been supposed. Similarly Beck⁸⁷ has found 10 positive reactions in 31 cases of internal ear disease in which there was no disease of the sound-conducting apparatus. In a recent examination (Noguchi test) of 128 cases of ear disease

81. Oiggaard: Wassermann-Reaktionens Betydning ved Hjerte og Karsygdomme, Høsp., Tids., 1909, No. 49. (Reviewed in Ztschr. f. Immunitätsforsch., 1910, II, 1068.)

82. Krefling, R.: Leichensera und die Wassermannsche Syphillisreaktion, Deutsch. med. Wchnschr., 1910, xxxvi, 366.

83. Cohen, M.: The Value of the Serodiagnosis of Syphilis in Ophthalmology: A Preliminary Report, Arch. Ophth., 1910, xxxix, 93.

84. Schumacher, G.: Die Serodiagnose der Syphilis in der Augenhellkunde nebst Bemerkungen über die Beziehungen der Tuberculose zur Syphilis bei Augenerleidn., Deutsch. med. Wchnschr., 1909, xxxv, 1915.

85. Hessberg, R.: Beiträge zur Bedeutung der Serodiagnose der Syphilis für die Augenhellkunde, Klin. Monatsbl. f. Augenh., 1910, xiviii, Beilageheft, p. 60.

86. Busch, H.: Wassermannsche Seroreaktion bei nervöser Schwerhörigkeit und Otosklerose, Beiträge Ohres, Nase, Halses, 1909, III, 42.

87. Beck, O.: Ueber die Erkrankungen des Inneren Ohrs und deren Beziehungen zur Wassermannschen Serumreaktion, Monatschr. f. Ohrenh. u. Laryngo-Rhinol., 1910, xlii, 28.

by E. P. Fowler⁸⁸ it was found that the greater number of positive reactions in adults were obtained in cases of nerve-deafness and chronic catarrhal disease of the middle ear.

Some opinions regarding the relationship of syphilis to ozena may have to be revised in the light of recent experience with the Wassermann reaction. The results thus far obtained would seem to indicate that syphilis plays little or no part in the etiology of this disease. Sobernheim⁸⁹ has recently examined 4 cases of ozena of long standing in which evidences of very recent syphilitic infection were present. The cases, as would be expected, gave a positive reaction. The same writer had previously tested 17 cases of ozena in all of which the results were entirely negative. Weinstein⁹⁰ obtained only negative results in examining 8 cases of ozena and the same results were found by Alexander⁹¹ in a series of 26 cases.

Additional light has been thrown on the intensely interesting problems of syphilitic heredity by recent investigations with the Wassermann reaction. Knoepfelmacher and Lehdorff⁹² in examining 116 apparently healthy mothers of syphilitic children, found positive reactions in 62 per cent. of the cases, corroborating the work of the others that had been done in this direction. The inference might be drawn that the mothers were suffering from latent syphilis, a fact which might offer an explanation of Colles' law. That the inference is not to be drawn from the results of the Wassermann reaction alone has been set forth by Baisch.⁹³ He also found a large proportion of his reactions in apparently healthy mothers of syphilitic infants, and thinks that such findings might be explained on theoretical grounds in three ways. In the first place, the mothers might have been victims of latent syphilis. In the second place, the mothers might have been healthy, the posi-

88. Fowler, E. P.: The Serodiagnostics of Syphilis in Its Relation to Disease of the Ear, *Ann. Otol., Rhinol. and Laryngol.*, 1910, xix, 367.

89. Sobernheim, W.: Ozaena und Syphilis: Neue Beobachtung, *Arch. f. Laryngol. u. Rhinol.*, 1909, xxli, 430.

90. Weinstein, J.: Ueber die Bedeutung der Wassermannschen Syphilisreaktion für die Rhino-Laryngologie, *Deutsch. med. Wchnschr.*, 1909, xxxv, 1696.

91. Alexander, A.: Serodagnostische Untersuchungen zur Frage der Beziehungen zwischen Ozaena und Syphilis, *Ztschr. f. Laryngol.*, 1909, l, 669.

92. Knoepfelmacher, W., and Lehdorff, H.: Das Collesche Gesetz, *Med. Klin.*, 1909, v, 1506.

93. Baisch, K.: Die Vererbung der Syphilis auf Grund serologischer und bakteriologischer Untersuchungen, *München. med. Wchnschr.*, 1909, lvi, 1929.

tive reaction being due to inhibitory substances that had been produced in the child and passed through the dividing wall of the placenta into the mother's circulation. In the third place, the mothers might have been immune to syphilis, assuming that the inhibitory substances represent immune bodies produced in either fetal or maternal organism and circulating in the mother's blood. To settle the question Baisch combined the serologic examination of the mother and child with examinations for the *Spirochæta pallida* in the placenta. He found in these clinically healthy women, giving a positive Wassermann reaction, that the spirochetes could be found in both fetal and maternal portions of the placenta as well as in the maternal circulation, apparently proving the first possibility, namely, that the mothers were the bearers of latent syphilis.

Speaking further for this explanation and against the possibility of the reaction being due to inhibitory bodies passing from the child to the mother, is the fact that the positive reaction in the mother does not disappear after the birth of the child. Furthermore, the reaction can be positive in the mother and negative in the child. Bruck has pointed out that a number of cases have been reported in which a syphilitic child gave a negative reaction at birth, and later when manifestations appeared the reaction became positive. In spite of this the mother at the time of the birth gave a positive reaction. In these cases a passage of the inhibitory bodies from child to mother was certainly impossible. The most difficult cases to explain would be the ones in which the mothers, in addition to being clinically healthy, gave a negative reaction while their offspring were shown to be undoubtedly syphilitic from demonstration of the presence of the spirochetes. It might be thought that in these cases we had to deal with pure paternal heredity, or the explanation might be found in the failure of the Wassermann test to show a positive reaction. The proof that the explanation lay in the failure of the test was apparent from the fact that in the negative as in the positively reacting mothers, spirochetes were found in both portions of the placenta and in the maternal circulation.

Not only may our ideas concerning Colles' law have to be revised, but also those concerning the law of Profeta, which says that apparently healthy children

of syphilitic parents are immune to syphilis, at least up to the time of puberty. The presence of a positive Wassermann reaction in a large number of these supposedly healthy children goes far to prove that here again the immunity to syphilis is only apparent.

That not only hereditarily syphilitic infants but also older children suffering from hereditary syphilis give a higher proportion of positive reactions has been shown by Bertin and Gayet.⁹⁴ In examining 25 undoubted cases of hereditary syphilis they found positive reactions in all but one case. Knoepfelmacher and Lehnendorff⁹⁵ also conclude that older heredo-syphilitic children give a positive Wassermann reaction more often than adults in the late stage of acquired syphilis.

The results obtained by the Wassermann test in studying the relationship of idiocy to syphilis do not entirely agree. From an examination of 200 cases Kellner, Clemenz, Bruckner and Rautenberg⁹⁶ found only 3 per cent. of positive reactions and conclude that syphilis does not play an important etiological rôle in idiocy. Lippmann,⁹⁷ who found 13.2 per cent. of positive reactions, thinks that syphilis is not to be considered as the cause of idiocy, even though it is safe to regard some forms of this condition as syphilitic. Atwood⁹⁸ in the study of 204 idiots (employing the Noguchi modification) found a positive reaction in 14.7 per cent. of the cases. Plaut from his experience is unwilling to draw any conclusions as to the relationship of idiocy to syphilis.

In their serologic investigations on dementia præcox, Roubinovitch and Levaditi⁹⁹ obtained only negative results and conclude that the cerebral changes characterizing this condition are not due to syphilis. In an examination of 109 cases of locomotor ataxia Frey¹⁰⁰ found 69 per cent. of positive reactions, and thinks that

94. Bertin and Gayet: Syphilis héréditaire et réaction de Wassermann, *Rev. de méd.*, 1910, xxx, 395.

95. Knoepfelmacher, W., and Lehnendorff, H.: Untersuchungen hereditärscher Kinder mittels der Wassermannschen Reaktion, *Das Gesetz von Profeta*, Wien, med. Wchnschr., 1909, lix, 2230.

96. Kellner, Clemenz, Bruckner and Rautenberg: Wassermannsche Reaktion bei Idiotie, *Deutsch. med. Wchnschr.*, 1909, xxxvi, 1827.

97. Lippmann, H.: Ueber den Zusammenhang von Idiotie und Syphilis, *München. med. Wchnschr.*, 1909, lvi, 2417.

98. Atwood, C. E.: Idiocy and Hereditary Syphilis, *THE JOURNAL A. M. A.*, Aug. 6, 1910, p. 464.

99. Roubinovitch and Levaditi: Rôle de la syphilis dans l'étiologie de la démence précoce, *Compt. rend. Soc. de biol.*, 1909, lxi, 880.

100. Frey, E.: Die Wassermannsche Reaktion und ihr Wert bei der Diagnose der Tabes, *Pest. med.-chir. Presse*, 1910, xiv, 116.

it can be affirmed from these results that tabes is a parasymphilitic disease.

The value of the Wassermann reaction for pathologic-anatomic diagnosis would appear to be still in some doubt in spite of several favorable contributions to the subject that have recently appeared. Seligman and Blume¹⁰¹ found the reaction positive in 8 cases of meso-ortitis productiva, in 3 cases of flat base of the tongue and in 7 out of 8 cases of aneurism. They consider the method to be an aid to pathologic-anatomic diagnosis. Glaser and Wolfsohn¹⁰² conclude from autopsy findings that the Wassermann reaction can give a correct diagnosis where neither history nor clinical manifestations show evidence of syphilis. The reaction was found positive by Schlimpert¹⁰³ in cases of mesaortitis (Heller), testicular nodes, flat tongue base and paresis. He states that the specificity of the reaction was in general upheld. In an examination of 100 cases Veszprémi¹⁰⁴ found 46 positive reactions, in 38 of which the reaction was justified by the post-mortem findings. None of the negative cases showed any evidence of syphilis. Examinations of pericardial, ascitic and hydrocele fluid and thoracic transudate gave practically the same results as when blood serum was used. Very unfavorable results were on the other hand obtained by Krefting,¹⁰⁵ who found 24 positive reactions in cases in which syphilis could probably be excluded. He therefore concludes that the Wassermann test with cadaver blood can give misleading results.

Finally it may be of interest to call attention to some recent serologic investigations tending to show the widespread infection of prostitutes by syphilis. Dreyer and Melrowsky¹⁰⁶ found the Wassermann reaction positive in 83 per cent. of prostitutes showing no clinical manifestations of syphilis. When the more delicate modification of Stern was used, the proportion was in-

101. Seligmann, E., and Blume, G.: Die Luesreaktion an der Leiche, Berl. klin. Wehnschr., 1909, xiv, 1116.

102. Glaser, F., and Wolfsohn, G.: Klinische Beobachtungen über die Wassermann-Neisser-Brucke'sche Reaktion und deren Kontrolle durch Sektionsresultate, Med. Klin., 1909, v, 1731.

103. Schlimpert, H.: Beobachtungen bei der Wassermann'schen Reaktion, Deutsch. med. Wehnschr., 1909, xxxv, 1386.

104. Veszprémi, D.: Die Bedeutung der Wassermann'schen Reaktion bei pathologisch-anatomischen Obduktionen, Centralbl. f. allg. Path. u. path. Anat., 1910, xxi, 193.

105. Krefting, R.: Leichensera und die Wassermann'sche Syphilisreaktion, Deutsch. med. Wehnschr., 1910, xxxvi, 366.

106. Dreyer, A., and Melrowsky, E.: Serodiagnostische Untersuchungen bei Prostituierten, Deutsch. med. Wehnschr., 1909, xxxv, 1698.

creased to nearly 90 per cent.. Seligmann and Pinkus¹⁰⁷ have also found positive reactions in 88 per cent. of prostitutes giving no history or symptoms of syphilis.

In conclusion it would seem that there has been some very substantial progress during the past year in the serum diagnosis of syphilis. The continued investigations on the Wassermann test have not only added much that is new to our knowledge, but have tended to confirm the view that the reaction is one of very great practical value. The results obtained in a number of other diagnostic tests for syphilis must at least be considered as encouraging.

SUMMARY

1. The various precipitation tests for the diagnosis of syphilis are too unreliable to be of much practical value.

2. The Schürmann color reaction has been extensively tried and found to be worthless.

3. The favorable results that have been claimed for the intradermic reaction are at least encouraging, as the performance of the test seems to be simple.

4. Excellent results have been claimed by Richard Weil for his cobra venom test. They are, however, somewhat lessened in value by the fact that very considerable experience is required to perform the reaction.

5. Further investigations are required to show whether the leuko-diagnosis, the antitryptic index or the meio-stagmin reaction can be used as diagnostic aids in syphilis. The results obtained with the Much-Holzmann reaction appear to be of no value.

6. The artificial antigens of Sachs and Rondoni, and of Schürmann for the Wassermann reaction have not succeeded in replacing the use of organ extracts.

7. The use of barium sulphate suggested by Wechselmann to remove the disturbing complementoids from the patient's serum has apparently given a greater proportion of positive reactions than those obtained by the original Wassermann method.

8. The use of urine in place of serum for the Wassermann reaction is not to be recommended.

107. Seligmann, E., and Pinkus, F.: Beiträge zur Theorie und Praxis der Wassermannschen Reaktion. Ztschr. f. Immunitätsforsch., 1910, v, 377.

9. No single modification has as yet entirely replaced the original Wassermann method. The modifications of Hecht and of Stern have apparently given good results abroad, while the Noguchi test has received almost universal recognition in America. The methods of Bauer and of Tschernogubow (second test) appear to be of much less value.

10. To the list of non-syphilitic diseases which at times give a positive Wassermann reaction, must apparently be added lupus erythematosus acutus. It has also been found that many cases give a positive reaction following ether narcosis.

11. The diagnostic value of a positive reaction is generally recognized. There is no general agreement as yet regarding the value of the test as a guide for treatment.

12. From recent serologic investigations it would appear that syphilis plays a very important rôle in the etiology of aortic insufficiency. Syphilis is probably of more importance in the causation of nerve-deafness than has been previously supposed. There is apparently little or no relation between syphilis and ozena.

13. A new field seems to have been opened by the Wassermann reaction for the discussion of the problem of the inheritance of syphilis and of the interpretation of the laws of Colles and Profeta.

14. In the field of pathologic-anatomic diagnosis the Wassermann reaction seems to be of considerable value.

15. Serologic examinations have shown that the percentage of syphilitic infections in prostitutes is extremely high.

616 Madison Avenue.

